

Appl. No. 09/641,104  
Amtd. Dated August 20, 2003  
Reply to Final Office Action of February 21, 2003

### AMENDMENTS TO THE SPECIFICATION:

Please replace the paragraph beginning at page 11, line 18, with the following rewritten paragraph:

Synthetic peptides from the N-terminal area of hTCF-4 with substitutions of the amino acid residues indicated were tested for their ability to inhibit the interaction between LEF-1 and  $\beta$ -catenin. The substitution of the acid amino acid residues of Asp10, Asp15 and Asp22 of TCF-4 by ~~aniline~~ alanine results in stopping the inhibition by the respective peptides. The substitution of Phe20 and Lys21 has the same effect. By a deletion an acid, minimum binding domain of TCF-4 for  $\beta$ -catenin of a length of 14 amino acids (Asp 10 up to Glu23) was identified.

Please replace the paragraph beginning at page 12, line 2, with the following rewritten paragraph:

A substitution of acid amino acid residues and of ~~phenyl-alanine~~ phenylalanine in the minimum binding domain of LEF-1 blocks the translocation of  $\beta$ -catenin into the cell nucleus.

Please add the following new paragraph describing figures 7-9 after the paragraph ending on line 3 of page 13 (before the line starting with "Tab 1:"):

Fig. 7:

Characterization of a hydrophobic pocket adjacent to the essential binding sites of  $\beta$ -catenin for LEF-1/TCF

A. View of the hydrophobic pocket at the molecule surface of  $\beta$ -catenin (RasMol). The pocket is flanked by amino acids marked in orange or yellow colours. The amino acid

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residues of the essential binding site for LEF/TCF are marked in blue colour. The respective amino acids have been marked.

B. Side view of hydrophobic pocket.

Fig. 8:

Substances binding in the hydrophobic pocket of  $\beta$ -catenin

A. Representation of the surface of the hydrophobic pocket region (Grasp). The amino acid residues of the essential binding site for LEF/TCF are marked in blue colour (for mutations blocking the interaction between  $\beta$ -catenin and LEF/TCF: Lys435, Arg 469 and His 470). In the  $\beta$ -catenin molecule one of the low-molecular substances binding in the pocket is represented.

Fig. 9:

Cefamandole as a representative of molecule class I inhibits the complex formation of LEF-1 and  $\beta$ -catenin in an ELISA.

Rising concentrations of cefamandole (15-250  $\mu$ M) result in a reduction of the complex formation of LEF-1 and  $\beta$ -catenin protein prepared recombinantly and purified in an ELISA ( $IC_{50}=25 \mu$ M).

Please add the following new paragraph after the paragraph ending on line 12 of page 13:

Tab. 3:

Substances potentially binding in the hydrophobic pocket ("drug list")

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Tab. 4:

“Positive list” of substances inhibiting the complex formation or  
stopping the inhibition by competition around the binding site in  
the pocket.

Please replace Tables 1 –4 with the replacement Tables 1–4 which has the translated German to  
English text. These are attached below.